REMARKS

Pending claims

Claims 10-43 are pending, claims 10-35 being withdrawn from consideration.

Claims 10-35 are canceled herein solely to expedite prosecution and without prejudice to pursuing these in continuing and other related applications. Claims 36 and 40 are amended and claims 44 and 45 are added herein. No new matter is presented by these claims. Support for the amended and newly added claims may be found throughout the specification, but at least in Figure 1, at page13, lines 2-11 and at page 16, lines 8-15.

Upon entry of this amendment and response, claims 36-45 are presented for examination.

Claims 36-43-Are Rejected Under 35 U.S.C. § 112, Second Paragraph

Claims 36-43 are rejected under 35 U.S.C. § 112, second paragraph because the Examiner asserts that the claims fail to particularly point out and claim the invention. The Examiner states that the claims are rendered indefinite by the phrase "substantially". Applicants respectfully traverse the rejection and submit that the meaning of the term would be well understood by those of ordinary skill in the art. However, solely to expedite prosecution of the application, the claims have been amended to remove this term. Accordingly, Applicants respectfully submit that the rejection is no longer proper and should be withdrawn.

Claims 36-43 Are Rejected Under 35 U.S.C. § 112, First Paragraph

Claims 36-43 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time that the application was filed had possession of the

claims invention. Applicants respectfully submit that the rejection is moot in view of the amendment to claims 36-43 which no longer contain the term "stationary". However, to the extent that the rejection would be applied to newly added claims 44 and 45, Applicants traverse the rejection.

In particular, Applicants' specification complies fully with § 112 because it reasonably conveys to one of skill in the field that the inventors had possession of the claimed subject matter as of the priority date. It is understood that when the USPTO reviews the sufficiency of the present disclosure, that there will be no obligation imposed for literal description of the claimed subject matter (*in haec verba*). See MPEP § 2163.02 (reporting that there is no such obligation). Instead, the test is that Applicant's specification must reasonably convey the inventive concept embodied in the claims to worker reading his case. Under that test, the specification fully satisfies the statutory requirements of 35 USC § 112, first paragraph. Figure 1, itself, in combination with the description of the Figure at page 13, lines 6-11, and page 16, lines 8-15 provides clear evidence that applicant was in possession of subject matter relating to the use of a stationary surface at the time of filing of the application. As held in *Vas-Cath Inc. v. Mahurkar* 19 U.S.P.Q.2d 1111, 935 F2d 1555 (Fed. Cir. 1991), both drawings and the text of the specification may be used to satisfy the written description requirement and confirm possession of an invention, and indeed that the drawings alone may be used to satisfy this requirement. Accordingly, Applicants respectfully submit that the rejection is improper and should be reconsidered and withdrawn.

Claims 36-43 Are Rejected Under 35 U.S.C. § 103

Claims 36-43 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,780,295 ("the '295 patent") taken with Steponkus, et al., *Nature* 34: 170-172, 1990 ("Steponkus"), Martino, et al., *Biology of Reproduction* 54: 1059-1069, 1966 ("Martino"), Yang, et al., *Theriogenology* 51: 178, 1999 ("Yang") and Papis, et al., *Theriogenology* 1: 173, 1999 ("Papis").

The Examiner asserts that the '295 patent discloses a method which comprises the step of suspending and rinsing biological material in solutions containing cryoprotectants, the step of

dropping the solutions with the biological material in a form of microdroplets and onto a solid cryogeneic surface which is cooled to about –160°C. The Examiner acknowledges that the '295 patent and Steponkus disclose substantially larger droplets than those claimed herein (i.e., 25-250 µl droplets are disclosed in the '295 patent and 20 µl droplets are disclosed in Steponkus) but states Martino discloses microdroplets having a size less than 1 µl for biological material comprising oocyytes, and that Yang and Papis disclose droplets of 10 µl and 6 µl, respectively. The Examiner asserts that the motivation to provide smaller droplets is provided in the '295 patent at column 6, lines 32-37 where the patent discloses that microdroplets on the order of 25 – 100 µm in diameter are preferred in order to achieve maximum cooling rates and short drying times.

Applicants traverse the rejection. The '295 patent provides no motivation go below the stated microdroplet range of 25-250 µl to provide a droplet which is 10 µl or less. Applicants further disagree that the required volume sizes can be extracted from the completely different techniques of Martino, Yang and Papis to modify the '295 patent. As stated by the Federal Circuit in *In re Fritch*, 23 U.S.P.Q.2d 1780, 1783 (Fed.Cir. 1992) (citing *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed.Cir. 1988) "[i]t is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious." *Id.*, at 1284. The '295 patent simply does not disclose nebulizers delivering biological materials in microdroplets of 10 µl or less and the secondary references do not remedy this deficiency.

Further, none of the methods disclose or suggest directly contacting microdroplets of 10 µl or less to a precooled *stationary* solid surface having a heat conductivity of greater than about 10 W/(m-k) at 20°C and a temperature of from about –150°C to about –180°C as required in new claims 44 and 45. The '295 patent requires a complex device with a rotating surface. The secondary references do not supply provide no motivation to modify this device to provide a *stationary solid surface* which is precooled. Papis describes dropping oocytes directly into *liquid* nitrogen or submerging a cryovial of embryos loaded with cryoprotectant *into liquid nitrogen,* i.e., Papis *does not disclose a stationary solid surface.* Yang reports dropping microdroplets of zygotes onto *liquid N_2 -filled* Petri dishes floating on liquid nitrogen, *also not a solid surface.* The surfaces described by Martino and

Steponkus are *not stationary* and *not precooled* during the vitrification process, rather biological material is placed on a surface which is *later* plunged into liquid nitrogen. To the extent that the surfaces taught by Martino and Steponkus are ever even momentarily stationary, they are not pre-cooled to a temperature of –150°C to about –180°C when contact between the biological material in the cryoprotectant solution and the surface occurs. Thus, the references combined do not result in the claimed invention and provide no motivation to achieve the claimed invention.

Additionally, the alleged motivation described by the Examiner for seeking lower volume sizes in the '295 patent merely further points out the differences between the method disclosed in the '295 patent and the methods claimed in claims 36-45. There is no drying required in the instant invention. This is reflected in the language of all of the claims that recite that vitrification solution is provided which has a concentration of cryoprotectant *so that the formation of ice in the contacting with said solid surface is prevented.* In contrast, the '295 patent clearly states that ice crystal formation occurs during the contact process (see, e.g. column 13, lines 60-66), in other words, that ice formation is *not* prevented upon contact. To compensate for the damaging effects of crystal formation, the '295 patent discloses using a complex drying step. None of the references cited by the Examiner, alone or in combination, describe a method in which vitrification occurs instantly in small microdroplets of a solution 10 µl or less upon contact with a precooled surface at a temperature of 150°C to about –180°C *without the formation of ice in the contacting with said solid surface* as claimed herein.

In further support of the non-obviousness of Applicants' claimed invention are the superior survival rates afforded by practicing the claimed method. In contrast to prior art methods, implementation of Applicants' claimed methods result in survival rates greater than 94% for oocytes in contrast to survival rates of 62% and 74% reported in the prior art (see page 14, lines 12-21). This difference is significance and unexpected and should be given weight in considering the patentability of Applicants' invention.

Accordingly, in view of the above arguments, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

CONCLUSION

Applicants submit that the claims are allowable and that the application is now in condition for allowance. Applicants respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Respectfully submitted,

Date: June 27, 2003

Dianne M. Rees, Ph.D.
(Reg. No: 45,281)
EDWARDS & ANGELL, LLP
P.O. Box 9169
Boston, MA 02209

Telephone: 617-439-4444
Customer No. 21874

BOS2_339212.1